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EXAMINER	
WANG, CHANG YU	
ART UNIT	**PAPER NUMBER**
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,649	TERENGHI ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-14* is/are pending in the application.

4a) Of the above claim(s) *7-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/01/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on December 4, 2006 is acknowledged. The traversal is on the ground(s) that all of the claims share the same special technical feature of a polyhydroxyalkanoate polymer in the form of a porous conduit wherein the polyhydroxyalkanoate polymer comprises 4-hydroxybutyrate. Applicant's arguments have been fully considered but they are not found persuasive. Since the device comprising a polyhydroxyalkanoate polymer in the form of a porous conduit wherein the polyhydroxyalkanoate polymer comprises 4-hydroxybutyrate is known in the art as set forth in the previous office action, it does not have a special technical feature. Therefore, claim 1 does not recite a special technical feature, defined by the PCT rules as a feature that defines a contribution over the prior art. Since the 1st claimed invention has no special technical feature, it cannot share a special technical feature with the other claimed inventions. Thus, Applicant's inventions do not have a single inventive concept and so lack unity of invention. Since Applicant's invention lacks unity of invention, the restriction requirement is based on the US practice. If the product is found allowable, the method of making and the method of using the products will be rejoined with the product as set forth in the previous office action.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 3-14 are pending. Claim 2 is canceled. Claims 7-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Claims 1, 3-6 are under examination in this office action.

Specification

The use of the trademarks Mylar®, NeuraGen Nerve Guide™ and Neurotube™ has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nerve regeneration device for nerves of the peripheral nervous system comprising a polyhydroxyalkanoate polymer in the form of a porous conduit wherein the polyhydroxyalkanoate polymer comprises 4-hydroxybutyrate, does not reasonably provide enablement for a nerve regeneration

device for all types of nerves as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

"There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue'. These factors include, but are not limited to:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)". See MPEP § 2164.01.

Claims 1, 3-6 are drawn to a nerve regeneration device comprising a polyhydroxyalkanoate polymer in the form of a porous conduit wherein the polyhydroxyalkanoate polymer comprises 4-hydroxybutyrate. Applicant describes a higher regeneration rate for PHA4400 (poly-4-hydroxybutyrate, P4HB) when compared

to PHB (poly-3-hydroxybutyrate) in a sciatic nerve transaction model wherein the nerve transaction is 10 mm in length. The sciatic nerve transaction model is a model for study of peripheral nerve regeneration. However, the claims are not limited to peripheral nerve regeneration. Applicant fails to provide sufficient guidance as to whether the claimed device could be used to regenerate all different types of nerves including nerves of the central nervous system since the regeneration in the central nervous system is still a challenge. Several molecules have been identified to inhibit remyelination in the CNS and axonal/neurite regeneration, including myelin-associated molecules such as Nogo, MAG, and proteoglycans in the extracellular matrix, (see p. 1052, 2nd col., Blight Nat. Neurosci. 2002. 5: 1051-4; p. 316, Schmidt et al. Annu. Rev. Biomed. Eng. 2003. 5: 293-347 and p. 450, 2nd col. Hoke et al. Nat. Clin. Pract. Neurol. 2006: 448-454). The nerve injury of the CNS regularly results in generating glial scars and demyelination, which inhibits nerve regeneration (Hoke et al. Nat. Clin. Pract. Neurol. 2006: 448-454). No single component is solely responsible for regeneration failure in the adult CNS (p. 624, Yiu et al. Nat. Rev. Neurosci. 2006. 7:617-627). Applicant is enabled for regenerating a peripheral nerve with a limited length of nerve transaction by a nerve regeneration device comprising 4-hydroxybutyrate. However, Applicant is not enabled for all types of nerve regeneration as broadly claimed since nerve regeneration of a long distant nerve transaction requires overcoming inhibiting neurite outgrowth of certain inhibitory molecules and enhancing neurite outgrowth and to coordinate multiple molecules among axonal/dendritic inhibitory molecules and axonal/dendritic attracting molecules to establish specific synaptic connection and plasticity. Applicant is also not

enabled for all nerve damage caused by all potential mechanisms since neither prior art nor the specification has provided any evidence that the nerve damage of the CNS can be repaired. Therefore, in view of the necessity of experimentation, the limited working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention as it pertains to a nerve regeneration device comprising a polyhydroxyalkanoate polymer in a form of a porous conduit wherein the polyhydroxyalkanoate polymer comprises 4-hydroxybutyrate.

Obviousness-Type Non-Statutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims1-34 of U.S. Patent No. 6610764, claims 1-4, 6-28 of US 6838493, claims 1-3, 5-20 of US 6548569, claims 1-4, 6-30 of US 6867247, claims 30, 35-61 of US 7179883. Claims 1, 3-6 of the instant application encompass a nerve regeneration device comprising a polyhydroxyalkanoate polymer in the form of a porous conduit wherein the polyhydroxyalkanoate polymer comprises 4-hydroxybutyrate and the conduit comprises nerve cells, growth factors or drugs. Claims 1-34 of '764 encompass a biocompatible polyhydroxyalkanoate composition comprising poly-4-hydroxybutyrate and the biocompatible composition comprises active agents including growth factors and drugs. Claims 1-4, 6-28 of '493 encompass a device comprising a biodegradable polyhydroxyalkanoate polymer composition comprising a polymer selecting from poly-4-hydroxybutyrate, poly-4-hydroxybutyrate-co-3-hydroxybutyrate, poly-4-hydroxybutyrate-co-2-hydroxybutyrate and copolymers thereof, and the composition also comprises active agents including growth factors and drugs. Claims 1-3, 5-20 of '569 encompass a biodegradable polyhydroxyalkanoate composition selecting from poly-4-hydroxybutyrate, poly-4-hydroxybutyrate-co-3-hydroxybutyrate, poly-4-hydroxybutyrate-co-2-hydroxybutyrate and copolymers thereof. Claims 1-4, 6-30 of '247 encompass a biocompatible polyhydroxyalkanoate composition comprising poly-4-hydroxybutyrate and the biocompatible composition comprises active agents including growth factors and drugs, and the device comprising the biocompatible composition for different medical uses including nerve regeneration. Claims 30, 35-61 of '883 encompass a device for different medical uses comprising a biodegradable

polyhydroxyalkanoate composition comprising poly-4-hydroxybutyrate and the device also comprises different drugs for medical use including nerve regeneration. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims recite the same composition comprising a polyhydroxyalkanoate polymer comprising 4-hydroxybutyrate. In addition, the poly-4-hydroxybutyrate encompasses 4-hydroxybutyrate with one or more different hydroxy acid units. The intended use for nerve regeneration is not given a patentable weight since the composition of the issued patents is the same as in the instant application and can perform the same function as in the instant claimed product. Thus, the instant and the issued patents claim a non-distinct invention of a biodegradable composition comprising a polyhydroxyalkanoate polymer that comprises 4-hydroxybutyrate.

Claims 1, 3-6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18, 21-25 of copending Application No. 10/835926 (US2004/0234576), which has a common assignee, and claims 1-8 of copending Application No. 11/193580 (US2006/0058470), which has a common assignee. Claims 1, 3-6 of the instant application encompass a nerve regeneration device comprising a polyhydroxyalkanoate polymer in the form of a porous conduit wherein the polyhydroxyalkanoate polymer comprises 4-hydroxybutyrate and the conduit comprises nerve cells, growth factors or drugs. Claims 1-18, 21-25 of '926 encompass a fiber comprising poly-4-hydroxybutyrate polymers and the device comprising one or more fibers comprising poly-4-hydroxybutyrate for different medical

uses including nerve regeneration. Claims 1-8 of '580 encompass a polymeric filament for a medical device comprising 4-hydroxybutyrate or copolymers thereof. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims recite the same composition comprising a polyhydroxyalkanoate polymer that comprises 4-hydroxybutyrate. In addition, the poly-4-hydroxybutyrate as recited in the claims also includes 4-hydroxybutyrate with one or more different hydroxy acid units. The intended use of the device comprising 4-hydroxybutyrate for nerve regeneration is not given patentable weight since the composition of the copending applications is the same as in the instant application and can perform the same function as in the instant claimed product. Thus, the instant and the issued patents claim a non-distinct invention of a biodegradable composition comprising a polyhydroxyalkanoate polymer that comprises 4-hydroxybutyrate.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

A search of inventors' names indicates that Applicant has filed several related applications. It is incumbent on the applicant to inform the office of all related subject matter and to file all related terminal disclaimers. See 37 CFR 1.56, Duty to disclose information material to patentability.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3-6 are rejected under 35 U.S.C. 102(a)/(e) as being anticipated by US 6548569 (issued on Apr 15, 2003, priority date Mar 25, 1999). US 6548569 teaches devices of tissue regeneration or nerve guidance/regeneration formed of biocompatible polyhydroxyalkanoates comprising poly-4-hydroxybutyrate as in claims 1 and 3 (see col. 4, lines 20-57; col.7, lines 31-35). '569 teaches a biodegradable device comprising a polyhydroxyalkanoate comprising 4-hydroxybutyrate in a form of porous conduit such as NEUROTUBE™ products as incorporated by the references such as US Pate NOs. 5735863, 5584885 and 5026381. US Patent No. '569 teaches the pore size of PHA is nanometers to 500μm in diameter as in claims 4-5 (co. 10, lines 31-42). '885 also teaches conduit comprising Schwann cells, growth factors and drugs as in claim 6 (see col.). Therefore, claims 1, 3-6 are anticipated by US 6548569.

Claims 1, 3-6 are rejected under 35 U.S.C. 102 (b) as being anticipated by each of the following individual references: US2002/0156150 (US Application No. 10/082954, published Oct 24, 2002) and US2002/017358 (US Application No. 10/136499, published Nov 21, 2002). The reasons for the rejection are provided as set forth above. Therefore, Claims 1, 3-6 are anticipated by each of the following individual references: US2002/0156150 and US2002/017358.

Claims 1, 3-6 are rejected under 35 U.S.C. 102(e) as being anticipated by each of the following individual references: U.S. Patent No. 6610764 (issued on Aug 26, 2003, priority date Nov 17, 1997), US 6838493 (issued on Jan 4, 2005, priority date Mar 25, 1999), US 6867247 (issued Mar 15, 2005, priority date Mar 25,1999), US 7179883 (issued on May 19, 2005, priority date Mar 25, 1999).

The applied references have a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the references, they constitute prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131. The reasons are provided in the section of Obviousness-Type Non-Statutory Double Patenting and as set forth above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/54593 (published Aug 2, 2001) in view of Martin et al. (2003. 16: 97-105 cited in the previous office action).

WO 01/54593 teaches a nerve regeneration conduit comprising biodegradable polymers selecting from polyhydroxyalkanoate, polyhydroxybutyric acid and polyesters (p. 14, claims 6-8). WO01/54593 teaches the conduit comprising Schwann cells or neurotrophic agents and the thickness of conduit is 5-200μm (p.2-4). WO01/54593 fails to teach 4-hydroxybutyrate and pore size of 5-500μm in diameter.

Martin et al. teaches poly-4-hydroxybutyrate is a polyester that belongs to the class of polyhydroxyalkanoate (PHA) and used for tissue regeneration (see p.97, 1st col. 1st paragraph; 2nd col. 1st paragraph). Martin et al. teach P4HB patches with a pore size

of 180-240μm, which meets the limitation recited in claims 4-5 (see p. 100, 1st col. 2nd paragraph). Martin et al. further teach that P4HB is more stable and useful for tissue engineering and PHA polymers including P3HB and its copolymers are successful in use of peripheral nerve repair (p. 105, 1st col., 2nd paragraph). The teachings of Martin et al. provide a motivation and expectation of success in using P4HB in peripheral nerve regeneration since PHA polymers have been used to generate a nerve regeneration conduit.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to combine the teachings of WO 01/54593 and Martin et al. to make a nerve regeneration conduit comprising PHA wherein the PHA comprises P4HB. The person of ordinary skill in the art would have been motivated to do so because PHA and P3HB have been used to successfully repair peripheral nerves and P4HB is more stable to hydrolysis in tissue engineering. One of ordinary skill in the art would have expected success in making a nerve regeneration device comprising PHA that comprises P4HB since PHA has been used to generate a nerve regeneration conduit and P4HB has a more stable property for tissue engineering.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang, Ph.D. whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CYW
January 30, 2007

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER